RESEARCH CENTRE

Inria Saclay Center at Institut Polytechnique de Paris

IN PARTNERSHIP WITH:

Institut Polytechnique de Paris

2022
ACTIVITY REPORT

Project-Team
M3DISIM

Mathematical and Mechanical Modeling with Data Interaction in Simulations for Medicine

IN COLLABORATION WITH: Laboratoire de Mécanique des Solides

DOMAIN

Digital Health, Biology and Earth

THEME

Modeling and Control for Life Sciences

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Project-Team M3DISIM

Creation of the Project-Team: 2016 June 01

Keywords

Computer sciences and digital sciences

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Other research topics and application domains

- B1.1.8. – Mathematical biology
- B1.1.9. – Biomechanics and anatomy
- B2.2.1. – Cardiovascular and respiratory diseases
- B2.6.2. – Cardiac imaging
- B2.6.3. – Biological Imaging

1 Team members, visitors, external collaborators

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- Philippe Moireau [Team leader, INRIA, Senior Researcher, HDR]
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2 Overall objectives

The research carried out in the MΞDISIM team has a rather global methodological perspective oriented towards biomechanics, encompassing mathematical modeling and analysis, inverse problems arising from model-data coupling, and the formulation and analysis of effective and reliable numerical procedures adapted to this overall program. We are also very keen on demonstrating the effectiveness and relevance of these methods in actual applications, usually by proof-of-concept studies carried out within various collaborations.

3 Research program

3.1 Multi-scale modeling and coupling mechanisms for biomechanical systems, with mathematical and numerical analysis

Over the past decade, we have laid out the foundations of a multi-scale 3D model of the cardiac mechanical contraction responding to electrical activation. Several collaborations have been crucial in this enterprise, see below references. By integrating this formulation with adapted numerical methods, we are now able to represent the whole organ behavior in interaction with the blood during complete heart beats. This subject was our first achievement to combine a deep understanding of the underlying physics and physiology and our constant concern of proposing well-posed mathematical formulations and adequate numerical discretizations. In fact, we have shown that our model satisfies the essential thermo-mechanical laws, and in particular the energy balance, and proposed compatible numerical schemes that – in consequence – can be rigorously analyzed, see [6]. In the same spirit, we have formulated a poromechanical model adapted to the blood perfusion in the heart, hence precisely taking into account the large deformation of the mechanical medium, the fluid inertia and moving domain, and so that the energy balance between fluid and solid is fulfilled from the model construction to its discretization, see [7].

3.2 Inverse problems with actual data – Fundamental formulation, mathematical analysis and applications

A major challenge in the context of biomechanical modeling – and more generally in modeling for life sciences – lies in using the large amount of data available on the system to circumvent the lack of absolute modeling ground truth, since every system considered is in fact patient-specific, with possibly non-standard conditions associated with a disease. We have already developed original strategies for solving this particular type of inverse problems by adopting the observer stand-point. The idea we proposed consists in incorporating to the classical discretization of the mechanical system an estimator filter that can use the data to improve the quality of the global approximation, and concurrently identify some uncertain parameters possibly related to a diseased state of the patient. Therefore, our strategy leads to a coupled model-data system solved similarly to a usual PDE-based model, with a computational cost directly comparable to classical Galerkin approximations. We have already worked on the formulation, the mathematical and numerical analysis of the resulting system – see [5] – and the demonstration of the capabilities of this approach in the context of identification of constitutive parameters for a heart model with real data, including medical imaging, see [3].

4 Application domains

As already emphasized in the team's objectives, we consider experimental studies and clinical applications as crucial, both for motivating our new modeling endeavors, and to validate the global modeling simulation chain, via the numerical simulation and inverse problems (for data-based estimation).

For instance, the translation of the modeling and data assimilation techniques developed in our team into cardiac clinical applications is pursued in two main directions: 1. Cardiac modeling for monitoring purposes in anesthesia and critical care medicine 2. Cardiac modeling in heart diseases. Concerning the clinical applications of lung modeling and data interaction, the team works for a better understanding of pulmonary fibrosis and with recent new research about COVID pulmonary infections. Another example is the clinical relevance of our modeling and characterization of the biomechanical behavior of the cornea.

Beyond medical applications, our general methods have applications in many industrial fields. For instance, our expertise in wave propagation and associated inverse problems have potential applications in non-destructive testing of structure.

5 Social and environmental responsibility

5.1 Impact of research results

5.1.1 AnaestAssist project and impact for anaesthesia

Unstable hemodynamics during general anaesthesia increases the risk of cardiac, renal and brain dysfunctions during the postoperative period, thus leading to a higher level of morbidity and mortality. To improve the patient's condition, learned societies therefore recommend monitoring the hemodynamics of the patient and having treatment strategies with quantitative objectives based on this monitoring. Currently, medical doctors have at their disposal some physiological signals (ECG, blood pressure) displayed on their monitor, and must rely on established practices and their experience to act in case of a dangerous drift.

The AnaestAssist project proposes to develop an augmented monitoring tool for anaesthesia. The proposed technology will introduce into the monitoring loop a predictive biophysical model, simulated in real time, and fed by the measured physiological signals. The model will be personalised for the patient, thus creating a digital twin of the patient's cardiovascular system. With this digital twin, physiological information that can cannot be measured or that can only be obtained with highly invasive methods will be computed in real time and treatment recommendations will be made. Our system will thus provide a much more complete vision of the patient's cardiovascular state and allow more informed and faster decisions. Eventually, the effects of drugs will be included in the model, which will make it possible to determine (through predictive modeling) adapted action recommendations, or even a real-time automatic drug administration loop. Our technology is expected to allow the medical staff to deliver a better treatment to the patient, to improve the patient's condition through a reduction of the risk related to general anaesthesia and a wiser exposition to drugs, and to reduce the costs for the health care system due to a lower rate of complications and shorter hospital stays.

The AnaestAssist project is intended to lead to a startup creation in the near future.

5.1.2 COVID research

In response to the ongoing COVID-19 pandemic caused by SARS-CoV-2, governments are taking a wide range of non-pharmaceutical interventions (NPI). These measures include interventions as stringent as strict lockdown but also school, bar and restaurant closures, curfews and barrier gestures, i.e. social distancing. Disentangling the effectiveness of each NPI is crucial to inform response to future outbreaks. To this end, we propose to develop a multi-level estimation of the French COVID-19 epidemic over a period of one year. This work performed with colleagues from project-teams Sistm and Monc among others has been published in [18] for the methodological aspects and in [17] for the applications to the COVID-19 pandemic.

More specifically in this work, we rely on a global extended Susceptible-Infectious-Recovered (SIR) mechanistic model of the infection including a dynamical (over time) transmission rate containing a Wiener process accounting for modeling error. Random effects are integrated following an innovative population approach based on a Kalman-type filter where the log-likelihood functional couples data across French regions. We then fit the estimated time-varying transmission rate using a regression model depending on NPI, while accounting for vaccination coverage, apparition of variants of concern (VoC) and seasonal weather conditions. We show that all NPI considered have an independent significant effect on the transmission rate. We additionally demonstrate a strong effect from weather conditions which decrease transmission during the summer period, and also estimate increased transmissibility of VoCs.

5.1.3 Withings

With the french compagny Withings, specialized in health monitoring solutions through connected devices (watch, balance, etc.), we propose to process the collected measurements by our data assimilation approaches based on the modeling of the underlying biophysical processes. These models of the cardiovascular system and the real-time estimation methods developed by the team are ideally suited to the distal data on cardiovascular functioning collected by Withings. New algorithms for estimating the physiology of subjects respecting the constraints of optimal regularization of signals, detection of defects by searching for causality, privacy on shared data will make it possible in the future to detect deterioration in the cardiovascular state of patients.

6 Highlights of the year

- M. Genet and S. Imperiale defended their Habilitation (HDR)
- ANR Kayo was granted to J.M. Allain on venous clots
- M. Genet and D. Chapelle are involved of the newly granted European project LF-Spiro3D

7 New software and platforms

7.1 New software

7.1.1 MoReFEM

Name: Modeling Research with the Finite Element Method

Keywords: HPC, Multiphysics modelling, Data assimilation

Functional Description: MoReFEM is a HPC finite element library for simulating multiphysics evolution problems like the ones encounter in cardiac modeling (electrophysiology, structure and fluid mechanics, transport-diffusion, wave equations)

URL: `https://gitlab.inria.fr/MoReFEM`

Contact: Sebastien Gilles

Participants: Sebastien Gilles, Jerome Diaz, Yves Le Tallec, Philippe Moireau, Dominique Chapelle, Chloe Giraudet, Giulia Merlini

7.1.2 HeartLab

Keywords: Computational geometry, Image analysis, Cardiac, Health, Simulation

Functional Description: The heartLab software is a library designed to perform both simulation and estimation of the heart mechanical behavior (based on various types of measurements, e.g. images).

Also included are geometric data and tools in the code to define cardiac anatomical models compatible with the simulation requirements in terms of mesh quality, fiber direction data defined within each element, and the referencing necessary for handling boundary conditions and estimation, in particular. These geometries are analytical or come from computerized tomography (CT) or magnetic resonance (MR) image data of humans or animals.

URL: `https://raweb.inria.fr/rapportsactivite/RA2013/m3disim/uid14.html`

Contact: Philippe Moireau

Participants: Radomir Chabiniok, Gautier Bureau, Martin Genet, Federica Caforio, Ustim Khristenko, Dominique Chapelle, Philippe Moireau

7.1.3 CardiacLab

Keywords: Cardiovascular and respiratory systems, Matlab, Real time

Functional Description: CardiacLab is a MATLAB toolbox allowing to perform “real-time” cardiac simulations using 0D models of the cardiovascular systems. Its modular development includes (1) a module integrating the mechanical dynamics of the cavity taking into account its particular geometry, (2) a module allowing to choose a micro-model of the cardiac contraction, (3) a module of phase management, (4) a circulation module based on Windkessel models or more advanced 1D flows models, and (5) a perfusion module. The objective of this code is threefold: (1) demonstrate to students, engineers, medical doctors, the interest of modeling in cardiac applications, (2) unify our original modeling developments with the possibility to evaluate them with previous team developments before integrating them into 3D complex formulations, and (3) explore some avenues pertaining to real-time simulat

Release Contributions: Addition of a mechanical formulation expressed analytically as a function of displacements

URL: `https://gitlab.inria.fr/M3DISIM/CardiacLab`

Contact: Philippe Moireau

Participants: Philippe Moireau, Dominique Chapelle, Francois Kimmig, Jerome Diaz, Sebastien Impériale, Martin Genet, Federica Caforio, Radomir Chabiniok, Arthur Le Gall, Matthieu Caruel, Jessica Manganotti

7.1.4 HELEN

Name: Heart Estimator For Live Evaluation in aNesthesia

Keywords: Low rank models, Dimensionality reduction, Cardiovascular and respiratory systems, Kalman filter, Dynamical system

Functional Description: Real-time fractional heartbeat simulation for on-board monitoring devices. Certified models and implementation with respect to numerical errors. Estimation of state and parameters by sequential filtering for model inversion.

Release Contributions: Launching simulations from option files in text format Choice of modeling components from the option file Simulation results exported in csv format and visualization module available. Modules for the direct problem and the inverse problem (Kalman filter type algorithm). Unit tests implemented and workflow implementation on Inria’s continuous integration platform. Non-regression tests implemented (integration test) and implementation of the workflow on Inria's continuous integration platform

Contact: Philippe Moireau

Participants: Laurent Steff, Sebastien Gilles, Francois Kimmig, Dominique Chapelle, Philippe Moireau, Marc Teyssier

7.1.5 AKILLES

Name: Agnostic Kalman Inference parraLLEl Strategies.

Keywords: Kalman filter, Data assimilation

Functional Description: This library concerns sequential data assimilation algorithms and more particularly of the Uscented Kalman Filter type (Normal, Reduced, Transformed etc.). The principle is to communicate the sigma-points representing the model instances via a message exchange library (here ZeroMQ). Thus each particle calculates in parallel with the others, and the core of the algorithm in C ++ can cooperate with models written in any language.

Contact: Philippe Moireau

Participants: Laurent Steff, Sebastien Gilles, Philippe Moireau

8 New results

8.1 Mathematical and Mechanical Modeling

8.1.1 A generic numerical solver for modeling the influence of stress conditions on guided wave propagation for SHM applications

Participants: André Dalmora *(correspondant)*, Alexandre Imperiale, Sébastien Imperiale, Philippe Moireau.

Structural Health Monitoring (SHM) proposes to use sensors and signal processing units in situ to assess structure integrity. One of the most attractive SHM techniques is ultrasonic guided waves. Guided waves propagate on large distances and interact with defects in the structure making damage detection possible. Modelling and simulation can be helpful tools for the design or the reliability assessment of SHM solutions. The currently available models developed for that purpose do not take into account the effect of operational conditions such as internal stresses. These conditions can modify wave propagation and therefore affect the interpretation of recorded signals. In our work we derive corresponding numerical methods for elastic wave propagation in an arbitrarily deformed medium. Any hyperelastic constitutive law can be considered. As the structures considered are usually thin, we avoided shear locking by using a shell formulation to solve the quasi-static problem representing the effects of structure loading. We fed the computed displacement into a spectral elements method (SEM) kernel to solve the time-domain linearized 3D elastodynamics problem representing the wave propagation. We validated our model for an isotropic aluminium plate under tensile forces using experimental data available in the literature. Additionally, we applied these numerical procedures to other realistic experiments illustrating the effects of stresses on ultrasonic guided wave propagation. We are also investigating the associated inverse problem with preliminary results on prestresses reconstruction.

8.1.2 Dimensional reduction of a poromechanical cardiac model for myocardial perfusion studies

Participants: Radomir Chabiniok, Bruno Burtschell, Dominique Chapelle, Philippe Moireau *(correspondant)*.

In the work [16], we adapt a previously developed poromechanical formulation to model the perfusion of myocardium during a cardiac cycle. First, a complete model is derived in 3D. Then, we perform a dimensional reduction under the assumption of spherical symmetry and propose a numerical algorithm that enables us to perform simulations of the myocardial perfusion throughout the cardiac cycle. These simulations illustrate the use of the proposed model to represent various physiological and pathological scenarios, specifically the vasodilation in the coronary network (to reproduce the standard clinical assessment of myocardial perfusion and perfusion reserve), the stenosis of a large coronary artery, an increased vascular resistance in the microcirculation (microvascular disease) and the consequences of inotropic activation (increased myocardial contractility) particularly at the level of the systolic flow impediment. Our results show that the model gives promising qualitative reproductions of complex physiological phenomena. This paves the way for future quantitative studies using clinical or experimental data.

8.1.3 Asymptotic analysis of wave propagation in thin incompressible plates

Participants: Zineb Ramiche *(correspondant)*, Sébastien Imperiale.

The objective of this project was to study the behavior of the wave propagation equation in the cornea characterized by two small parameters η (related to the plate thickness) and δ (related to the quasi-incompressibility). Our approach is based on an asymptotic analysis of the solution $u_{\eta,\delta}$ involving multi-scales, represented by the two small parameters δ and η. The question that arises is whether or not the order in which we make the parameters tend to zero has an influence on the solution of the limit problem $u_{0,0}$. We derive the solution of the limit problem in the plate (i.e. the limit δ goes to zero) $u_{0,\eta}$ then make η tend to zero. Afterwards, we define the solution of the limit problem in an incompressible tissue (i.e. the limit η goes to zero) $u_{\delta,0}$ then make δ tend to zero. We show that the two limits commute. In fact, our analysis extends beyond this illustrative process, since we show that $u_{\delta,\eta}$ converges to a well defined $u_{0,0}$ for any path in the plane (η,δ).

8.1.4 Analysis of a linearized poromechanics model for incompressible and nearly incompressible materials

Participants: Mathieu Barré *(correspondant)*, Céline Grandmont *(Inria Paris, COMMEDIA)*, Philippe Moireau.

Biological tissues can be seen as porous media in which elastic fibers (such as the heart muscle, lung parenchyma, gray matter) and incompressible viscous fluids (blood, lymph, cerebrospinal fluid) are in interaction. Recently, a new model based on mixture theory was proposed to represent biological tissues perfusion. This is a fully dynamical model in which the fluid and solid equations are strongly coupled through the interstitial pressure. As such, it generalizes Darcy, Brinkman and Biot equations of poroelasticity. In previous works, the mathematical and numerical analysis of this model was performed for a compressible porous material.

Here, we focus on the nearly incompressible case with a semigroup approach that also allows to prove the existence of weak solutions. We show the existence and uniqueness of strong and weak solutions in the incompressible limit, which corresponds to the physiological regime and for which a non-standard divergence constraint arises. Due to the special form of the coupling, the underlying problem is not coercive. Nevertheless, by using the notion of T-coercivity, we obtain stability estimates and well-posedness results. Our study also provides guidelines to propose a stable and robust approximation of the problem with mixed finite elements. In particular, we recover an inf-sup condition independent of the phase field. Finally, we investigate numerically the elliptic regularity of the associated steady-state problem and illustrate the sensitivity of the solution with respect to the various model parameters.

An article corresponding to this work [13] was published in *Evolution Equations and Control Theory*.

8.1.5 The T-coercivity approach for mixed problems

Participants: Mathieu Barré *(correspondant)*, Patrick Ciarlet *(Inria Saclay, POEMS)*.

Classically, the well-posedness of variational formulations of mixed linear problems is achieved through the inf-sup condition. In [32], we propose an alternative framework to study such problems by using the T-coercivity approach. This is a constructive approach that leads to the design of suitable approximations in a simple way. In general, the derivation of the uniform discrete inf-sup condition for the approximate problems stems straightforwardly from the study of the original problem. To support our view, we solve a series of classical mixed problems with the T-coercivity approach. Among others, the celebrated Fortin Lemma appears naturally in the numerical analysis of the approximate problems.

8.1.6 Multiscale mechanical model based on patient-specific geometry: Application to early keratoconus development

Participants: Chloé Giraudet, Jérôme Diaz, Patrick Le Tallec, Jean-Marc Allain *(correspondant)*.

Keratoconus is a pathology of the cornea associated with tissue thinning and a weakening of its mechanical properties. However, it remains elusive which aspect is the leading cause of the disease. To investigate this question, we combined a multiscale model with a patient-specific geometry in order to simulate the mechanical response of healthy and pathological corneas under intraocular pressure. The constitutive behavior of the cornea is described through an energy function which takes into account the isotropic matrix of the cornea, the geometric structure of collagen lamellae and the quasi-incompressibility of the tissue. A micro-sphere description is implemented to take into account the typical features of the collagen lamellae as obtained experimentally, namely their orientation, their stiffness and their dispersion, as well as the their unfolding stretch, at which they start to provide a significant force. A set of reference parameters is obtained to fit experimental inflation data of the literature. We show that the most sensitive parameter is the unfolding stretch, as a small variation of this parameter induces a major change in the corneal apex displacement. The keratoconus case is then studied by separating the impact of the geometry and that of the mechanics. We computed the evolution of the SimK (a clinical indicator of cornea curvature) and elevation maps: we were able to reproduce the reported changes of SimK with pressure only by a mechanical weakening, and not by a change in geometry. More specifically, the weakening has to target the lamellae and not the matrix. The mechanical weakening leads to elevations close to early stage keratoconus, but our model lacks the remodeling component to couple the change in mechanics with changes in geometry. Still, these findings indicate that new methods for early diagnosis of keratoconus should focus on the detection of a mechanical weakening, and that stiffening treatments should be appropriate. This work was published in [20].

8.1.7 Multi-scale model of the lung

Participants: Mahdi Manoochehrtayebi, Martin Genet *(correspondant)*, Dominique Chapelle.

We are developing a multi-scale model of the lung that can mimic the lung behavior on the macroscopic scale and the microscopic one. We use the macroscopic model developed in the PhD of Cécile Patte (supervised by Dominique Chapelle and Martin Genet), which represents the relation between the stress, strain, and pore pressure at the macroscopic scale. Besides, we have developed a micromechanical model based on the microstructure developed during the first year. So far, we have obtained two models on the microscopic and macroscopic scale which can be compared to each other. We are also using our micromechanical model to create a framework based on finite elements, with which we can obtain the global response of the microstructure for any input. In 2022, this work has been presented at the CMBE conference in Milan, and also at GDR Mécabio Santé.

8.1.8 Uncertainty quantification in personalized pulmonary mechanics

Participants: Alice Peyraut, Martin Genet *(correspondant)*.

Idiopathic Pulmonary Fibrosis (IPF) is an interstitial lung disease whose mechanisms of evolution are poorly understood, making it difficult to diagnose and treat. The development of a physical model of the lungs, able to integrate patient data, could prove useful for the investigation of IPF and provide doctors with an efficient tool for prognosis and diagnosis.

One of the main challenges for the development of a personalized model is to formulate an appropriate material law representing accurately the constitutive behavior of the lungs. The constants involved in this law being highly patient-dependent, the question of their actual identifiability based on clinical data is central for the development of our personalized lung model. We therefore developed a statistical pipeline to perform a quantitative study of the identifiability of those material constants.

This pipeline relies on the construction of a cost function, measuring the difference between a synthetic displacement field (obtained with the model run with reference parameters values, to which random Gaussian noise is added) and the displacement field obtained with the model for given parameter values. The estimation is then performed by optimizing the cost function, here using the standard direct search Nelder-Mead method, starting from a random value. The optimization is performed for many realizations of noise, until convergence of the obtained distribution.

For any level of noise, our method provides the estimation error for the stiffness parameter: for large SNR, the optimization always converges toward the exact parameter value, whereas for small SNR the obtained parameters are far away from the ground truth. Thus, our pipeline allows to quantify the identifiability of the various parameters depending on the noise present on the measures and to estimate the error performed during the estimation process.

The results obtained illustrate that the pipeline we developed can be used as a tool to improve the estimation process, and therefore our personalized lung model.

8.1.9 Upscaling of nonlinear multiscale structures

Participants: Patrick Le Tallec *(correspondant)*.

Predicting the long term evolution of the fuel assemblies inside a nuclear reactor is capital for operational and safety purposes. This study started in 2017 has been concluded in 2022 by a PhD defense and one scientific publication [23]. A companion paper has been accepted for publication more recently. During this study, a general strategy combining Domain Decomposition and Nonuniform Transformation Field Analysis (NTFA) has been developed and validated for the simulation of nuclear fuel assemblies at the scale of a full nuclear reactor and of a two years nuclear cycle. The model at subdomain level solves the full elastic problem but with a reduced nonlinear loading, based on simplified boundary conditions, reduced creep flow rules, projected sign preserving contact conditions, and a NTFA-like reduced friction law to get the evolution of each slipping mode. With this loading reduction, the local solution can be explicitly obtained from a small set of precomputed elementary elastic solutions. The numerical tests indicate that considerable cost reduction (by a factor of 50 to 1000) can be achieved while preserving engineering accuracy.

8.1.10 Statistically equivalent surrogate material models

Participants: Patrick Le Tallec *(correspondant)*.

Manufactured materials usually contain random imperfections due to the fabrication process, e.g., the 3D-printing, casting, etc. These imperfections significantly affect the effective material properties and result in uncertainties in the mechanical response. Numerical analysis of the effects of the imperfections and the uncertainty quantification (UQ) can be often done by use of digital stochastic surrogate material models. We have developed a new flexible class of stochastic surrogate models depending on a small number of parameters and a calibration strategy ensuring that the constructed model fits to the available observation data, with a special focus on two-phase materials. The surrogate models are constructed as the level-set of a linear combination of an intensity field representing the topological shape and a Gaussian perturbation representing the imperfections, allowing for fast sampling strategies. The mathematical design parameters of the model are related to physical ones and thus easy to interpret. The calibration of the model parameters is performed using progressive batching sub-sampled quasi-Newton minimization, using a designed distance measure between the synthetic samples and the data. Then, employing a fast sampling algorithm, an arbitrary number of synthetic samples can be generated to use in Monte Carlo type methods for prediction of effective material properties. In particular, we illustrate the method in application to UQ of the elasto-plastic response of an imperfect octet-truss lattice which plays an important role in additive manufacturing.

8.1.11 Varying thin filament activation in the framework of the Huxley'57 model

Participants: François Kimmig *(correspondant)*, Matthieu Caruel, Dominique Chapelle.

Muscle contraction is triggered by the activation of the actin sites of the thin filament by calcium ions. It results that the thin filament activation level varies over time. Moreover, this activation process is also used as a regulation mechanism of the developed force. Our objective is to build a model of varying actin site activation level within the classical Huxley'57 two-state framework. This new model is obtained as an enhancement of a previously proposed formulation of the varying thick filament activation within the same framework. We assume that the state of an actin site depends on whether it is activated and whether it forms a cross-bridge with the associated myosin head, which results in four possible states. The transitions between the actin site states are controlled by the global actin sites activation level and the dynamics of these transitions is coupled with the attachment-detachment process. A preliminary calibration of the model with experimental twitch contraction data obtained at varying sarcomere lengths is performed. This work was published in [22].

8.1.12 A quasistatic poromechanical model of the lungs

Participants: Cécile Patte, , Martin Genet *(correspondant)*, Dominique Chapelle.

The lung vital function of providing oxygen to the body heavily relies on its mechanical behavior, and the interaction with its complex environment. In particular, the large compliance and the porosity of the pulmonary tissue are critical for lung inflation and air inhalation, and the diaphragm, the pleura, the rib cage and intercostal muscles all play a role in delivering and controlling the breathing driving forces. In the paper [25], we introduce a novel poromechanical model of the lungs. The constitutive law is derived within a general poromechanics theory via the formulation of lung-specific assumptions, leading to a hyperelastic potential reproducing the volume response of the pulmonary mixture to a change of pressure. Moreover, physiological boundary conditions are formulated to account for the interaction of the lungs with their surroundings, including a following pressure and bilateral frictionless contact. A strategy is established to estimate the unloaded configuration from a given loaded state, with a particular focus on ensuring a positive porosity. Finally, we illustrate through several realistic examples the relevance of our model and its potential clinical applications.

8.1.13 On the structural origin of the anisotropy in the myocardium: Multiscale modeling and analysis

Participants: Nicole Tueni, Jean-Marc Allain *(correspondant)*, Martin Genet.

Due to structural heterogeneities within the tissue, the myocardium displays an orthotropic material behavior. However, the link between the microstructure and the macroscopic mechanical properties is still not fully established. In particular, if it is admitted that the cardiomyocyte organization induces a transversely isotropic symmetry, the relative role in the observed orthotropic symmetry of cardiomyocyte orientation variation and perimysium collagen “sheetlet” structure, two mechanisms occurring at different scales, is still a matter of debate. In order to shed light on this question, we designed a multiscale model of the myocardium, bridging the cell, sheetlet and tissue scales. More precisely, we compared the macroscopic anisotropy obtained by homogenization of different mesostructures consisting in cardiomyocytes and extracellular collageneous layers, also taking into account the variation of cardiomyocyte and sheetlet orientations on the macroscale, to available experimental data. This study confirms the importance of sheetlets layers in assuring the tissue’s anisotropic response, as cardiomyocytes-only mesostructures cannot reproduce the observed anisotropy. Moreover, our model shows the existence of a size effect in the myocardial tissue shear properties, which will require further experimental analysis. This work was published in [26].

8.1.14 Reduced left ventricular dynamics modeling based on a cylindrical assumption

Participants: Martin Genet *(correspondant)*, Jérôme Diaz, , Dominique Chapelle, , Philippe Moireau.

Biomechanical modeling and simulation is expected to play a significant role in the development of the next generation tools in many fields of medicine. However, full-fledged finite element models of complex organs such as the heart can be computationally very expensive, thus limiting their practical usability. Therefore, reduced models are much valuable to be used, e.g., for pre-calibration of full-fledged models, fast predictions, real-time applications, etc.. In this work, focused on the left ventricle, we develop a reduced model by defining reduced geometry & kinematics while keeping general motion and behavior laws, allowing to derive a reduced model where all variables & parameters have a strong physical meaning. More specifically, we propose a reduced ventricular model based on cylindrical geometry & kinematics, which allows to describe the myofiber orientation through the ventricular wall and to represent contraction patterns such as ventricular twist, two important features of ventricular mechanics. Our model is based on the original cylindrical model of [Guccione, McCulloch, & Waldman 1991; Guccione, Waldman, & McCulloch 1993], albeit with multiple differences: we propose a fully dynamical formulation, integrated into an open-loop lumped circulation model, and based on a material behavior that incorporates a fine description of contraction mechanisms; moreover, the issue of the cylinder closure has been completely reformulated; our numerical approach is novel as well, with consistent spatial (finite element) and time discretizations. Finally, we analyse the sensitivity of the model response to various numerical and physical parameters, and study its physiological response.

8.2 Numerical Methods

8.2.1 Stabilization of the high-order discretized wave equation for data assimilation problems

Participants: Tiphaine Delaunay *(correspondant)*, Sébastien Imperiale, Philippe Moireau.

The objective of this work is to propose and analyze numerical schemes to solve data assimilation problems by observers for wave-like hyperbolic systems. The observer strategies using available measurements are becoming popular to improve the quality of numerical simulations of physical phenomena. The design of observers for these systems is now classical at the continuous level. The efficiency of these observers relies on the proof of the exponentially stable character of the underlying system when we add the dissipative term linked to the observations. This exponential stability depends on observability inequalities where the energy of the system is proven to be controlled by the observations. To demonstrate these inequalities, several methods exist in the literature: the multiplier method (introduced by J-L Lions as early as the 1980s), spectral methods, Carleman estimates and micro-local analysis. For 1D problems, the multiplier approach is very natural and provides near-optimal results. Unfortunately, the multiplier method is incompatible with the discretization needs. Indeed, with- out modification of the classical finite element methods used, the exponential stability (uniformly in h, the discretization step) is not preserved at the discrete level because of the presence of spurious waves.

8.2.2 Numerical modelling of transient elastographic measurements in the cornea

Participants: Giulia Merlini, Jean-Marc Allain, Sébastien Imperiale.

Dynamic elastography is a fundamental technique to study the local mechanical property of the tissues, such as cornea. It is based on in-vivo tracking of shear waves propagation as a result of a transient stimulation. In nearly incompressible materials, such as the cornea, the shear waves are 150 times slower than the compression waves. The incompressibility and the double-scale of the phenomena make the FE approximation difficult. The objective of this study is to propose an efficient scheme to obtain a reliable modelling of transient elastography measurements applied to the cornea and to improve tissue characterisation techniques.

The acoustic radiation force is a common mechanical stimulation to generate low-frequency shear waves. In order to model the resulting shear-wave propagation phenomenon, we propose a FE approximation with high-order spectral elements together with a Mass Lumping approach. This allows to avoid the inversion of mass matrix at each time step by computing an approximate value of the mass integrals with a numerical integration formula (Gauss-Lobatto rule).

Incompressibility is a well-known problem in FE approximation with pure displacement method, due to locking, ill-conditioning of the stiffness matrix and incorrect pressures approximations. To overcome these limitations, we use a mixed formulation with the introduction of the pressure as a local variable defined on each element. The approximation of the displacement and the pressure field are performed with $\mathbb{Q}_4 - \mathbb{Q}_2^{disc}$ elements.

For the time discretisation, the explicit leapfrog scheme shows high efficiency and second-order accuracy. However, the time step is strongly decreased by the velocity of the compression wave. In this study, we propose a strategy inspired by local time-stepping method. The contribution of pressure wave is computed explicitly in an inner loop. While maintaining stability and accuracy, we obtain a fully explicit algorithm that is more efficient in terms of CPU time compared to the standard LF scheme.

We have performed simulations of elastic wave propagation on a homogeneous isotropic cornea with a CPU time of 75 minutes. In preliminary simulations we achieve a computational time three times lower, with a relative error on the displacement of the order of 4% compared to the LF scheme. The natural extension of this work is to perform simulations taking into account the pre-stress state with a non-linear law and then integrate the model with the anisotropic behavior related to the lamellar structure of the cornea.

8.2.3 An efficient numerical method for time domain electromagnetic wave propagation in co-axial cables.

Participants: Akram Beni-Hamad *(Inria Saclay, POEMS)*, Sébastien Imperiale *(correspondant)*, Patrick Joly *(Inria Saclay, POEMS)*.

In the work [14], we construct an efficient numerical method to solve 3D Maxwell's equations in coaxial cables. Our strategy is based upon a hybrid explicit-implicit time discretization combined with edge elements on prisms and numerical quadrature. One of the objectives is to validate numerically generalized Telegrapher's models that are used to simplify the 3D Maxwell equations into a 1D problem.

8.3 Inverse Problems

8.3.1 Reduced-order Kalman observer in metric spaces: application to wildfire propagation

Participants: Gaël Le Ruz *(correspondant)*, Philippe Moireau.

The goal of this work is to implement a reduced-order Kalman filter (ROKF) using the Hausdorff distance as a measure of the discrepancy between fire fronts. First, we investigate the description of simple models for the propagation of fire fronts at the regional or gigascopic scale. We focus mainly on a Lagrangian description: the envelope model. We then proceed with the implementation of the classical Kalman filter, using a simplified linearized model of fire front propagation. In order to work with the original envelope model, we study the metric space of shapes induced by the Hausdorff distance and propose a definition of a ROKF in this space by analogy with the classical ROKF in Euclidean spaces.

8.3.2 Solving inverse source wave problem: from observability to observer design

Participants: Tiphaine Delaunay *(correspondant)*, Sébastien Imperiale, Philippe Moireau.

The objective of this work is to propose a practical method using observers to estimate a source term of a wave equation, from internal measurements in a subdomain. The first part of the work consists in proving an identifiability result from classical observability conditions for wave equations. We deduce that the source reconstruction is an ill-posed inverse problem of order 2. This inverse problem is solved using a sequential strategy that is proven to be equivalent to a minimization of a cost functional with Tikhonov regularization.

8.3.3 Kernel representation of Kalman observer and associated H-matrix based discretization

Participants: Matthieu Aussal *(Inria Saclay, IDEFIX)*, Philippe Moireau *(correspondant)*.

In deterministic estimation, applying a Kalman filter to a dynamical model based on partial differential equations is theoretically attractive, but solving the associated Riccati equation leads to a so-called curse of dimensionality for its numerical implementation. In the work [12], we propose to entirely revisit the theory of Kalman filters for parabolic problems where additional regularity results prove that the Riccati equation solution belongs to the class of Hilbert-Schmidt operators. The regularity of the associated kernel then allows to proceed to the numerical analysis of the Kalman full space-time discretization in adapted norms, hence justifying the implementation of the related Kalman filter numerical algorithm with H-matrices typically developed for integral equations discretization.

8.3.4 Estimation for dynamical systems using a population-based Kalman filter – Applications in computational biology

Participants: Annabelle Collin *(Inria Bordeaux, MONC)*, Philippe Moireau, Melanie Prague *(Inria Bordeaux, SISTM, correspondant)*.

Estimation of dynamical systems – in particular, identification of their parameters – is fundamental in computational biology, e.g., pharmacology, virology, or epidemiology, to reconcile model runs with available measurements. Unfortunately, the mean and variance priors of the parameters must be chosen very appropriately to balance our distrust of the measurements when the data are sparse or corrupted by noise. Otherwise, the identification procedure fails. One option is to use repeated measurements collected in configurations with common priors – for example, with multiple subjects in a clinical trial or clusters in an epidemiological investigation. This shared information is beneficial and is typically modeled in statistics using nonlinear mixed-effects models. In the work [17], we present a data assimilation method that is compatible with such a mixed-effects strategy without being compromised by the potential curse of dimensionality. We define population-based estimators through maximum likelihood estimation. We then develop an equivalent robust sequential estimator for large populations based on filtering theory that sequentially integrates data. Finally, we limit the computational complexity by defining a reduced-order version of this population-based Kalman filter that clusters subpopulations with common observational backgrounds. The performance of the resulting algorithm is evaluated against classical pharmacokinetics benchmarks. Finally, the versatility of the proposed method is tested in an epidemiological study using real data on the hospitalisation of COVID-19 patients in the regions and departments of France.

8.3.5 Using Population Based Kalman Estimator to Model COVID-19 Epidemic in France: Estimating the Effects of Non-Pharmaceutical Interventions on the Dynamics of Epidemic

Participants: Annabelle Collin *(Inria Bordeaux, MONC)*, Boris Hejblum *(Inria Bordeaux, SISTM)*, Laurent Lehot *(Inria Bordeaux, SISTM)*, Carole Vignals *(Inria Bordeaux, SISTM)*, Rodolphe Thiébaut *(Inria Bordeaux, SISTM)*, Philippe Moireau, Melanie Prague *(Inria Bordeaux, SISTM, correspondant)*.

In response to the COVID-19 pandemic caused by SARS-CoV-2, governments have adopted a wide range of non-pharmaceutical interventions (NPI). These include stringent measures such as strict lockdowns, closing schools, bars and restaurants, curfews, and barrier gestures such as mask-wearing and social distancing. Deciphering the effectiveness of each NPI is critical to responding to future waves and outbreaks. To this end, we first develop a dynamic model of the French COVID-19 epidemics over a one-year period. We rely on a global extended Susceptible-Infectious-Recovered (SIR) mechanistic model of infection that includes a dynamic transmission rate over time. Multilevel data across French regions are integrated using random effects on the parameters of the mechanistic model, boosting statistical power by multiplying integrated observation series. We estimate the parameters using a new population-based statistical approach based on a Kalman filter, used for the first time in analysing real-world data. We then fit the estimated time-varying transmission rate using a regression model that depends on the NPIs while accounting for vaccination coverage, the occurrence of variants of concern (VoC), and seasonal weather conditions. We show that all NPIs considered have an independent significant association with transmission rates. In addition, we show a strong association between weather conditions that reduces transmission in summer, and we also estimate increased transmissibility of VoC. This work was published in [17].

8.3.6 Discrete-time formulations as time discretization strategies in data assimilation

Participants: Philippe Moireau *(correspondant)*.

Data assimilation combines control theory and scientific computing to propose a set of methods for coupling dynamic models and data sequences for estimation and prediction in all engineering domains. Data assimilation naturally raises the question of how the developed control and optimization methods interact with the discretization of the underlying physical models, in particular their temporal discretization. We present in the work [28] some of the best known techniques developed for discrete-time models, which are essentially based on a mechanism involving model prediction on the one hand and data correction on the other. We show that they can be considered as specific discretizations of the data assimilation strategies proposed for continuous-time models in the sense of a discretization-and-then-control approach. This paradigm justifies the stability of these prediction-correction schemes, paving the way for convergence properties and justifying their popularity in practice.

8.3.7 Mortensen Observer for a class of variational inequalities - Lost equivalence with stochastic filtering approaches.

Participants: Louis-Pierre Chaintron, , Philippe Moireau *(correspondant)*.

We address in the work [34] the problem of deterministic sequential estimation for a nonsmooth dynamics in $\mathbb{R}^+$ governed by a variational inequality, as illustrated by the Skorokhod problem with a reflective boundary condition at 0. For smooth dynamics, Mortensen introduced an energy for the likelihood that the state variable produces – up to perturbations disturbances – a given observation in a finite time interval, while reaching a given target state at the final time. The Mortensen observer is the minimiser of this energy. For dynamics given by a variational inequality and therefore not reversible in time, we study the definition of a Mortensen estimator. On the one hand, we address this problem by relaxing the boundary constraint of the synthetic variable and then proposing an approximated variant of the Mortensen estimator that uses the resulting nonlinear smooth dynamics. On the other hand, inspired by the smooth dynamics approach, we study the vanishing viscosity limit of the Hamilton-Jacobi equation satisfied by the Hopf-Cole transform of the solution of the robust Zakai equation. We prove a stability result that allows us to interpret the limiting solution as the value function associated with a control problem rather than an estimation problem. In contrast to the case of smooth dynamics, here the zero-noise limit of the robust form of the Zakai equation cannot be understood from the Bellman equation of the value function arising in Mortensen's deterministic estimation. This may unveil a violation of equivalence for non-reversible dynamics between the Mortensen approach and the low noise stochastic approach for nonsmooth dynamics.

8.4 Experimental Assessments

8.4.1 3D-DIC in cornea shows a complex exchange of liquid during inflation assays

Participants: Chloé Giraudet, , Jean-Marc Allain *(correspondant)*.

To characterize the mechanical response of the human cornea under a wide range of pressures with a view to building a reference deformation profile for identification processes, we tested twenty human corneas under three different mechanical loadings: (i) Creep tests at physiological pressure to mimic transplant, (ii) inflation tests to characterize the mechanical response of the cornea under a wide range of pressures, (iii) creep tests at high pressure to capture the time dependent behavior of the cornea. Throughout the tests, 2- and 3-Dimensional Optical Coherence Tomography (OCT) images were taken and analyzed using Digital Image/Volume correlation (DIC/DVC).

At physiological pressure, the cornea inflates, and three distinct zones appear with different levels of deformation. During inflation test, the same three zones and the same profile of deformation have been observed, but the deformation is no longer positive anymore: the cornea is in compression in the middle and anterior layers. Our measurements of apex displacement with pressure during this test are comparable to those found by Elsheikh's group. Creep tests at high pressure point out the time-dependency of the mechanical response of the cornea, which compresses more and more with time. This can be due to the pumping out of the endothelium, which would become active with time at high pressure, or to an imbalance in the osmotic pressure.

In order to better understand the mechanical response of the cornea under pressure, a simplified analytical model was built in which the tissue is represented as an elastic material with varying Young's modulus and subjected to osmotic pressure. However, this model does not reproduce the experimental data, where the change in volume seems to start in the middle of the cornea – and not at the border.

8.4.2 Reconstruction of Voigt striae in cornea

Participants: Qian Wu, Jean-Marc Allain *(correspondant)*.

We investigate the organization of the Voigt striae in cornea, as observed under OCT. As striae are dark gray thin lines in a light gray noisy image, they are easy to observe but quite difficult to segment. So, we developped a suitable segmentation procedure. Then, we have developped an approach to reconstruct the 3D planes created by the striae. We have observed that the striae do not seem affected by the inflation tests, even at a pressure much larger than the physiological one. Thus, the exact physiological role of these structures remains elusive as they are normally supposed to disappear for cornea under pressure, as a way to accommodate the structure deformation.

8.4.3 Effect of decellularization on trachea mechanical properties

Participants: Jean-Marc Allain *(correspondant)*.

Tracheal replacement is a surgical technique that consists in removing a pathological part of the patient's native trachea and replacing it with a tubular structure with similar biomechanical and biological properties. It is needed when the patient's native trachea is affected by a pathology requiring a resection of more than 50% of the tracheal length in adults and 30% in children. In humans, the trachea consists of cartilaginous rings superimposed on each other (between fifteen and twenty) and connected by fibrous tissue. The cartilaginous rings are shaped like a horseshoe. It is this complex organisation that provides at the same time the extensibility of the trachea in the axial direction, and a higher stiffness in the radial direction. One of the key difficulties in tracheal replacement is to obtain a substitute that preserves these properties, while being immunocompatible. Immunocompatibility is achieved by removing totally or partly the cells of the tissue, so that it becomes acceptable for the receiver immune system. In the case of trachea, it has been shown that total decellularization induces a weakening of the cartilaginous rings, and that the trachea collapses in the expiration. We have tested the mechanical properties of normal and partially decellularized trachea, frozen or fresh, to compare the evolution of the mechanical properties. To do so, we have done traction tests and inflation tests. The inflation tests were done inside a microCT, so that we can observe the change of volume (and possible) collapse of the trachea. We concluded that partly decellularized trachea have properties close of native ones in the physiological range, but they are sligthly less extensible in the radial direction. For pressures beyond the physiological range, decellularized trachea seems to have more leaks and an easier collapse. These results, obtained on few trachea, need to be confirmed on a larger number of samples.

8.5 Clinical Applications

8.5.1 Estimation of regional pulmonary compliance in idiopathic pulmonary fibrosis based on personalized lung poromechanical modeling

Participants: Cécile Patte, Dominique Chapelle, Martin Genet *(correspondant)*.

Pulmonary function is tightly linked to the lung mechanical behavior, especially large deformation during breathing. Interstitial lung diseases, such as idiopathic pulmonary fibrosis (IPF), have an impact on the pulmonary mechanics and consequently alter lung function. However, IPF remains poorly understood, poorly diagnosed, and poorly treated. Currently, the mechanical impact of such diseases is assessed by pressure-volume curves, giving only global information. In the paper [24] we developed a poromechanical model of the lung that can be personalized to a patient based on routine clinical data. The personalization pipeline uses clinical data, mainly computed tomography (CT) images at two time steps and involves the formulation of an inverse problem to estimate regional compliances. The estimation problem can be formulated both in terms of “effective”, i.e., without considering the mixture porosity, or “rescaled”, i.e., where the first-order effect of the porosity has been taken into account, compliances. Regional compliances are estimated for one control subject and three IPF patients, allowing to quantify the IPF-induced tissue stiffening. This personalized model could be used in the clinic as an objective and quantitative tool for IPF diagnosis.

8.5.2 Quantification of left ventricular strain and torsion by joint analysis of 3D tagging and cine MR images

Participants: Ezgi Berberoğlu, , Martin Genet *(correspondant)*.

Cardiovascular magnetic resonance (CMR) imaging is the gold standard for the non-invasive assessment of left-ventricular (LV) function. Prognostic value of deformation metrics extracted directly from regular SSFP CMR images has been shown by numerous studies in the clinical setting, but with some limitations to detect torsion of the myocardium. Tagged CMR introduces trackable features in the myocardium that allow for the assessment of local myocardial deformation, including torsion; it is, however, limited in the quantification of radial strain, which is a decisive metric for assessing the contractility of the heart. In order to improve SSFP-only and tagged-only approaches, we propose in the paper [15] to combine the advantages of both image types by fusing global shape motion obtained from SSFP images with the local deformation obtained from tagged images. To this end, tracking is first performed on SSFP images, and subsequently, the resulting motion is utilized to mask and track tagged data. Our implementation is based on a recent finite element-based motion tracking tool with mechanical regularization. Joint SSFP and tagged images registration performance is assessed based on deformation metrics including LV strain and twist using human and in-house porcine datasets. Results show that joint analysis of SSFP and 3DTAG images provides better quantification of LV strain and twist as either data source alone.

8.6 AnaestAssist project

Participants: François Kimmig *(correspondant)*, Dominique Chapelle, , Philippe Moireau, .

Unstable hemodynamics during general anesthesia increases the risk of cardiac, renal and brain disfunctions during the postoperative period, thus leading to a higher level of morbidity and mortality. To improve the patient’s condition, learned societies therefore recommend monitoring the hemodynamics of the patient and having treatment strategies with quantitative objectives based on this monitoring.

Currently, medical doctors have at their disposal some physiological signals (ECG, blood pressure) displayed on their monitor, and must rely on established practices and their experience to act in case of a dangerous drift.

The AnaestAssist project proposes to develop an augmented monitoring tool for anesthesia. The proposed technology will introduce into the monitoring loop a predictive biophysical model, simulated in real time, and fed by the routinely measured physiological signals. The model will be personalized for the patient, thus creating a digital twin of the patient's cardiovascular system. With this digital twin, physiological information that can cannot be measured or that can only be obtained with highly invasive methods will be computed in real time and treatment recommendations will be made. Our system will thus provide a much more complete vision of the patient's cardiovascular state and allow more informed and faster decisions. Eventually, the effects of drugs will be included in the model, which will allow to determine (through predictive modelling) adapted action recommendations, or even a real-time automatic drug administration loop. Our technology is expected to allow the medical staff to deliver a better treatment to the patient, to improve the patient condition through a reduction of the risk related to general anesthesia and a wiser exposition to drugs, and to reduce the costs for the health care system due to a lower rate of complications and shorter stays of the patients at the hospital.

The AnaestAssist project is intended to lead to a startup creation in the near future.

The AnaestAssist team coordinated the response to several calls for proposal at the national and European levels in order to find fundings for the project next phase of development. As Inria, it participated to the construction of the 3-PLOS project led by our partner team of the anesthesia department of Lariboisière Hospital (AP-HP) in response to a Horizon Europe framework programm call. In doing so, it joined an international consortium made up of industrial partners: Philips France, Philips Electronics, Roche Diagnostics International and 4Teen4 Pharmaceuticals ; clinical partners: AP-HP, NHS Lothian and Karolinska University Hospital; academic partners: Université des Patients (Sorbonne Université), Universität Ulm, the Univerisity of Edinburgh and Universität Basel.

The AnaestAssist team submitted the MAUS project to the "Bernoulli Lab challenge" call, along with the anesthesia department of Lariboisière Hospital (AP-HP) and the Inria team COMMEDIA. The project MAUS was not selected.

The AnaestAssist team also built with the same partners the project CAPTAIN in response to a call of AP-HP research and innovation department. The evaluation phase of this call is ongoing.

The HΞLEN code constitutes a step towards the realization of the proof of concept of the AnaestAssist solution functioning in real time. Enhancements of the code were performed during the year : new valve model elements have been implemented, we introduced a launcher script, and we completed the embedded Kalman filter implementation.

Progresses have also been made on the user interface of the AnaestAssist product. A prototype of monitoring interface has been designed with the specialized agency DiciDesign.

9 Bilateral contracts and grants with industry

9.1 Bilateral contracts with industry

- Metyos company. Study of a skin injection device.

- CEA List. Collaboration contract arround A. Dalmora PhD work.

9.2 Bilateral grants with industry

- AMIES Grant with Withings compagny. Collaboration on data assimilation from connected devices measurements.

10 Partnerships and cooperations

10.1 International initiatives

10.1.1 Participation in other International Programs

- European Innovation Council (EIC) grant: V|LF-Spiro3D (PI: Xavier Maître, CNRS/Paris-Saclay University, 3.3M€).

10.2 National initiatives

10.2.1 Sachems

Participants: Sébastien Imperiale, Philippe Moireau, Andre Dalmora.

Structural Health Monitoring (SHM) consists of integrating sensors into a high-stakes structure (aircraft, nuclear power plant, wind turbine, etc.) to monitor its state of health in real time and thus anticipate maintenance operations. The project entitled "SACHEMS" ("SAClay High-end Equipment for the Monitoring of Structures"), as it was funded in 2019 under the SESAME system of the Ile-de-France region, aims to create a federative platform for research and innovation for the SHM, allowing the development of complete SHM systems and to deploy them on the application cases provided by industrial end users. This platform brings together both academic teams and industrial end-users. It offers to the public laboratories involved the possibility of carrying out research in close collaboration with industrial partners.

10.2.2 ANR

- **ANR JCJC LungManyScale (383 k€)**

  Participants: Martin Genet, Philippe Moireau, Dominique Chapelle, Madhi Manoochehrtayebi.

  The lungs' architecture and function are well characterized; however, many fundamental questions remain (e.g., there is no quantitative link between tissue- and organ-level material responses), which represent real health challenges (e.g., Idiopathic Pulmonary Fibrosis is a poorly understood disease, for which a mechanical vicious cycle has been hypothesized, but not demonstrated). The general objective of this project is twofold: (i) scientifically, to better understand pulmonary mechanics, from the alveola to the organ in health and disease; (ii) clinically, to improve diagnosis and prognosis of patients through personalized computational modeling. More precisely, This project aims at developing a many-scale model of the pulmonary biomechanics, linked by computational nonlinear homogenization. The model will integrate the experimental and clinical data produced by partners, through an estimation pipeline that will represent augmented diagnosis and prognosis tools for the clinicians.

- **ANR ODISSE, (154 k€)**

  Participants: Philippe Moireau, Sébastien Imperiale, Tiphaine Delaunay.

  Motivated by some recent developments from two different fields of research, that is, observer design for finite-dimensional systems and inverse problems analysis for some PDE systems, the ODISSE project aims at developing rigorous methodological tools for the design of estimation algorithms for infinite-dimensional systems arising from hyperbolic PDE systems.

- **ANR SIMR (97 k€)**

  Participants: Philippe Moireau, Dominique Chapelle, Jérôme Diaz, Martin Genet.

  SIMR is a multi-disciplinary project seeking a better understanding of the biophysical mechanisms involved in mitral valve (MV) regurgitation diseases, to improve decision-making in patients by helping to determine the optimal timing for surgery. This project aims at facing this major issue with the following main two objectives: (1) Evaluate the biophysical consequences of MV repair and (2) Design numerical tools for cardiac hemodynamics, fluid-structure interaction and myocardium biomechanics to provide an in silico counterpart of the in vivo data obtained by tension measurement and imaging.

- **ANR AAP RA-COVID-19 SILICOVILUNG (55k€)**

  Participants: Martin Genet, Collin Laville.

  It is currently impossible to predict the evolution of severe COVID19-induced lung pathologies, in particular towards pulmonary fibrosis. A patient-specific model of lungs at 2-3 months after the acute stage will be used to seek mechanical indicators that may be valuable to predict the lung state after one year.

- **ANR Elastoheart (212k€)**

  Participants: Philippe Moireau, Sébastien Imperiale, Dominique Chapelle.

  The objective of this project is to develop a comprehensive mathematical and numerical modeling (direct and inverse) of 3D Shear-Wave (SW) propagation in cardiac realistic physiological models, and to demonstrate in vivo that shear velocity can assess important cardiac function and characteristics in experimental pathological models and in patients.

- **ANR CorMecha (191k€)**,

  Participants: Jean-Marc Allain.

  This project aims at: (i) setting up an atlas of cornea 3D structure from the sub-micrometer scale (intra-lamellar organization of collagen fibrils) to the millimeter-centimeter scale, (ii) accurately measuring the biomechanical properties linked to this structure in physiological conditions and in various pathological conditions, and (iii) building a model of corneal biomechanics based on these microstructural and macroscopic data in order to provide insight into the role of specific stromal structures. It relies on the highly original combination of well-controlled inflation device and state-of-the-art imaging setups, mainly polarization-resolved second harmonic generation microscope. Specific bioimage informatics tools and pipelines will be developed to process the very large data sets (Gb to Tb) generated by this new device and quantify clinically-relevant parameters of interest. Advanced statistical analysis of the series of clinical, structural and mechanical data obtained on the same cornea will then be performed for normal, keratoconic and photo-ablated corneas. The ultimate goals are twofold: (i) to translate the structural features observed with advanced research microscopes into easily-detectable features using commonly used techniques in clinical ophthalmology, in order to enable the diagnosis of structural defects related to defective mechanical properties; (ii) to develop a patient-specific simplified model to serve as a predictive tool by clinicians, mainly to improve refractive surgery procedures.

10.2.3 Other funding

- AMIES Project WithCardiacModels, in partnership with Withings company (98k€)

Participants: Philippe Moireau, Jérôme Diaz, François Kimmig, Dominique Chapelle.

Connected objects are now emerging as an effective tool for non-invasive monitoring of the general state of health day and night. In order to process the generated data streams, many signal processing and learning algorithms are required to reconstruct actionable outputs about the user's health. Many objects providing interesting cardiovascular information for the general public already exist on the market, such as the Withings Scanwatch, which measures an ECG and detects atrial fibrillation.

In this project, we propose to process the measurements collected by data assimilation approaches based on the modeling of the underlying biophysical processes. These models of the cardiovascular system and the real-time estimation methods developed by the M3DISIM team are ideally suited to the distal data on cardiovascular functioning collected by Withings. New algorithms for estimating the physiology of subjects respecting the constraints of optimal regularization of signals, detection of defects by searching for causality, privacy on shared data will make it possible tomorrow to detect deterioration in the cardiovascular health of heart failure patients, for example.

11 Dissemination

11.1 Promoting scientific activities

11.1.1 Scientific events: organisation

Member of the organizing committees

- M. Genet, co-organiser of the GdR MécaBioSanté annual workshop

Member of the conference program committees

- P. Moireau member of the scientific committee, Colloque Ile de Sciences "Jumeaux Numériques" on digital twins

11.1.2 Journal

Member of the editorial boards

- D. Chapelle, member of the editorial board of journal *Computers & Structures*
- D. Chapelle, member of the editorial board of journal *ESAIM:M2AN*
- P. Le Tallec, member of the editorial board of journal *Computer Methods in Applied Mechanics and Engineering*
- P. Le Tallec, member of the editorial board of journal *Computer & Structures*
- P. Moireau, guest editor for the journal Maths-in-Action

Reviewer - reviewing activities

- J.M. Allain, reviewer for “Acta Biomateriala” (twice) and “Journal of the Mechanical Behavior of Biomedical Materials” (twice)
- D. Chapelle, reviewer for “Computers & Structures” (x3) and for “CMAME”
- M. Genet, reviewer for “Journal of Biomechanics”
- S. Imperiale, reviewer for “MathematicS In Action”, “Advances in Computational Mathematics”, JCP, SIAM - JSC
- F. Kimmig, reviewer for “Journal of computational biology” and “ESAIM:Procs”
- P. Moireau, reviewer for OCAM, M2AN, JCP

11.1.3 Invited talks

- D. Chapelle, invited speaker at 28th Nordic Congress of Mathematicians, Aalto University, Finland (August 18-21)
- M. Genet, invited keynote at the World Congress in Biomechanics, Taipei, Taiwan.
- M. Genet, invited presentation at the UTC-IPP Biomechanics Day.
- P. Le Tallec, “From Domain Decomposition to Model Reduction for Large Nonlinear Structures” Congrès pour honorer la mémoire de Roland Glowinski (Paris, 5-8 juillet 2022)
- P. Moireau, invited speaker at Seminaire LJLL (28/01), Laboratoire Mathématiques d’Orsay (17/03), for the 4th Training Event of projet européen GW4SHM (30/06) and Colloquium MAP5 Paris Descartes (18/12).

11.1.4 Leadership within the scientific community

- J.M. Allain, Member of the Société de Biomécanique
- J.M. Allain, Member of the European Society of Biomechanics
- M. Genet, Member of the Francophone Biomechanics Society
- M. Genet, Member of the French Computational Mechanics Association (CSMA)

11.1.5 Scientific expertise

- J.M. Allain, Reviewer for SNSF (Canada)
- J.M. Allain, Reviewer for Tec21 (Grenoble University)
- M. Genet, Reviewer for ANR
- M. Genet, Reviewer for ADUM
- P. Moireau, Vice President of the Jury ANR CE 46 2021-2022

11.1.6 Research administration

- J.M. Allain, Scientific Advisory Board, chair BioMecAM
- J.M. Allain, in charge of the axis « mécanique et matériaux pour le bio » at the Fédération Francilienne de Mécanique
- D. Chapelle, scientific head of the joint AP-HP–Inria laboratory "Daniel Bernoulli"
- D. Chapelle, member of the steering committee of the interdisciplinary center "Engineering for Health" (E4H) of IPP
- S. Imperiale. Member of the CE (Commission d'évaluation) at Inria
- P. Le Tallec, Dean of the bachelor program at Ecole Polytechnique.
- P. Moireau, Member of the LMS board
- P. Moireau, Member of the Commission scientifique and technique,Corps des Mines
- P. Moireau, Member of the steering committee of Department of Mathematics, Institut Polytechnique de Paris

11.2 Teaching - Supervision - Juries

11.2.1 Teaching

- All-level: J.-M. Allain, referent for disability at Ecole polytechnique, France
- Bachelor: J.-M. Allain, Academic advisor for mechanics at the Bachelor program Ecole Polytechnique, France
- Bachelor: J.-M. Allain, “Classical mechanics”, 24h, B2, Ecole Polytechnique, France
- Bachelor: M. Barré and T. Delaunay, "MA103 – Introduction aux EDP et à la méthode des différences finies", 14h, B3, ENSTA Paris, France
- Bachelor: S. Imperiale, “MA102 – Analyse pour les EDP”, 24h, B3, ENSTA ParisTech, France
- Bachelor: G. Merlini, “Modal de mécanique”, Xh, (L1), École Polytechnique, France
- Bachelor: A. Peyraut, “Maths in Practice Calculus”, 32h, L1, Ecole Polytechnique, France
- Master: J.-M. Allain, “Statistical mechanics: application to cell motility”, 20h, M2, Ecole Polytechnique, France
- Master: J.-M. Allain, “Introduction à la mécanique des milieux continus”, 30h, M2, Ecole Polytechnique, France
- Master: J.-M. Allain, “Biosolids”, 20h, M2, Ecole Polytechnique, France
- Master: M. Barré and T. Delaunay, “ANN201 – La méthode des éléments finis“, 14h, M1, ENSTA Paris, France
- Master: D. Chapelle, “MSE303 - Modélisation mathématique et estimation en biomécanique cardiaque – De la théorie aux applications médicales”, 9h, M2, Université Paris-Saclay and Institut Polytechnique de Paris, France
- Master: M. Genet, “Numerical methods in (solid) mechanics”, 54h, M1, École Polytechnique, France
- Master: M. Genet, “Model-Data interaction in mechanics”, 40h, (M1), École Polytechnique, France
- Master: M. Genet, “Ingénierie biomédicale basée sur la simulation mécanique : application à la fibrose pulmonaire”, 2h, (M2 B2PRS), Université Paris-Saclay

- Master: S. Imperiale, “MAP-ANA1 – Introduction à l’analyse fonctionnelle”, 12h, M1, ENSTA ParisTech, France
- Master: S. Imperiale, “AMS306 – Techniques de discrétisation avancées pour les problèmes d’évolutions”, 18h, M2, Université Paris-Saclay, France
- Master: P. Moireau, “AMS305 – Complétion de données et identification dans les problèmes gouvernés par des équations aux dérivées partielles”, 16h, M2, Université Paris-Saclay, France
- Master: P. Moireau, “MSE303 - Modélisation mathématique et estimation en biomécanique cardiaque – De la théorie aux applications médicales”, 16h, M2, Université Paris-Saclay and Institut Polytechnique de Paris, France
- Master: A. Peyraut, “Collective Scientific Projects (PSC)”, 16h, M1, Ecole Polytechnique, France

11.2.2 Supervision

- M2: A. Gaubert, “Augmented hemodynamic monitoring for patients under general anesthesia using a digital twin: focus on the activation function”, supervisors: F. Kimmig and F. Vallée, Université Paris-Est Créteil, Defended June 28
- M2: G. Le Ruz “Observateur de Kalman réduit dans des espaces métriques : application à la propagation de feux de forêts”, supervisor: P. Moireau, Defended Sept 2021
- M2: S. Bihoreau “Luenberger observers for electromagnetic characterization of objects”, supervisor: A. Collin and C. Poignard from Inria-Bordeaux Monc and S. Imperiale and P. Moireau.
- PhD defense: J. Manganotti, “Mathematical modeling and numerical simulation of left heart hemodynamics”, supervised by S. Imperiale and P. Moireau.
- PhD defense: Bertrand Leturcq, "Réductions de modèles thermomécaniques non-linéaires pour l’évaluation des déformations du cœur de réacteur", supervised by P. Le Tallec.
- PhD defense: Chloé Giraudet, "Mécanique multi-échelle de la cornée saine et pathologique", supervised by P. Le Tallec and J. M. Allain.
- PhD defense: Maria Gusseva, "Patient-specific cardiovascular biomechanical modeling to augment interpretation of clinical data and assist planning interventions for patients with congenital heart disease", supervised by R. Chabiniok and D. Chapelle
- PhD defense: E. Berberoglu, “Magnetic Resonance Imaging of Myocardial Strain and Image-Guided Computational Mechanics of the Heart”, defended in 03/2022, supervised by M. Genet and S. Kozerke (ETH Zurich)
- PhD in progress: T. Delaunay, “Adaptative observers for propagative systems and associated discretization: formulation and analysis”, started 2020, supervised by S. Imperiale and P. Moireau.
- PhD in progress: A. Dalmora, “ Modeling and estimation by data-assimilation of pre-stresses in non destructive testing experiments”, started 2020, supervised by A. Imperiale, S. Imperiale and P. Moireau.
- PhD in progress: M. Barré, “Mathematical framework for biological tissue perfusion modeling and simulation”,started 2020, supervised by C. Grandmont from Inria-Paris - Commedia and P. Moireau.
- PhD in progress: G. Le Ruz, “Observers in constrained spaces - from formulations to applications”, started oct. 2022, supervised by D. Lombardi from Inria-Paris - Commedia and P. Moireau.
- PhD in progress: L.P. Chaintron, “Large deviations and control problems under constraints, application to multi-scale modeling of cardiac muscle.”, started sept. 2020, supervised by J. Reygnier from Ecole des Ponts

- PhD in progress: Qian Wu, “Cornea biomechanics”, started oct. 2022; supervised by J.M. Allain.
- PhD in progress : Matheus de Lorenz, Approches multi-échelles de l’adhérence des pneumatiques sur route mouillée », started april 2021, supervised by P. Le Tallec.
- PhD in progress: M. Manoochertayebi, “Manyscale modeling of lung poromechanics”, started Nov. 2020, supervisors: M. Genet, A. Bel-Brunon (INSA-Lyon) and D. Chapelle
- PhD in progress: A. Peyraut, “Modeling and estimation of lung poromechanics”, started Dec. 2021, supervisor: M. Genet

11.2.3 Juries

- J. M. Allain, PhD Jury of B. Eydan, Université de Lyon, PhD Advisor: J. Molimard, jan 2022.
- J. M. Allain, PhD Jury of C. Piao, Université de Montpellier, PhD Advisor: P. Royer and C. Wagner-Kocher, dec 2022.
- J. M. Allain, PhD referee of K. K. Dwidedi, Indian institut of technology Ropar, PhD Advisor: N. Kumar.
- M. Genet, PhD Jury of Giulia Bellezza, INRIA Bordeaux & Université de Bordeaux, sept. 2022.

11.3 Popularization

- M. Barré, volunteer and board member of Animath, a non-profit association promoting math towards the young and the general public. Coordination team member of the French training program for International Mathematical Olympiads.
- M. Barré, in charge of a scientific activity at the *Fête des Sciences* organized by IP Paris, October 8th.
- P. Moireau, in the scientific committee of the popularization conference "Jumeaux Numériques" (Digital Twin) promoted by the association Ile de Science.

12 Scientific production

12.1 Major publications

[1] J. Albella Martínez, S. Imperiale, P. Joly and J. Rodríguez. ‘Solving 2D linear isotropic elastodynamics by means of scalar potentials: a new challenge for finite elements’. In: *Journal of Scientific Computing* (2018). DOI: 10.1007/s10915-018-0768-9. URL: https://hal.inria.fr/hal-01803536.

[2] M. Caruel, P. Moireau and D. Chapelle. ‘Stochastic modeling of chemical-mechanical coupling in striated muscles’. In: *Biomechanics and Modeling in Mechanobiology* (2018). DOI: 10.1007/s10237-018-1102-z. URL: https://hal.inria.fr/hal-01928279.

[3] R. Chabiniok, P. Moireau, P.-F. Lesault, A. Rahmouni, J.-F. Deux and D. Chapelle. ‘Estimation of tissue contractility from cardiac cine-MRI using a biomechanical heart model’. English. In: *Biomechanics and Modeling in Mechanobiology* 11.5 (2012), pp. 609–630. DOI: 10.1007/s10237-011-0337-8. URL: http://hal.inria.fr/hal-00654541.

[4] D. Chapelle and K. Bathe. *The Finite Element Analysis of Shells - Fundamentals - Second Edition*. English. Computational Fluid and Solid Mechanics. Springer, 2011, p. 410. DOI: 10.1007/978-3-642-16408-8. URL: http://hal.inria.fr/hal-00654533.

[5] D. Chapelle, N. Cîndea and P. Moireau. ‘Improving convergence in numerical analysis using observers - The wave-like equation case’. English. In: *Mathematical Models and Methods in Applied Sciences* 22.12 (2012). DOI: 10.1142/S0218202512500406. URL: http://hal.inria.fr/inria-00621052.

[6] D. Chapelle, P. Le Tallec, P. Moireau and M. Sorine. 'An energy-preserving muscle tissue model: formulation and compatible discretizations'. English. In: *International Journal for Multiscale Computational Engineering* 10.2 (2012), pp. 189–211. DOI: `10.1615/IntJMultCompEng.2011002360`. URL: `http://hal.inria.fr/hal-00678772`.

[7] D. Chapelle and P. Moireau. 'General coupling of porous flows and hyperelastic formulations – From thermodynamics principles to energy balance and compatible time schemes'. In: *European Journal of Mechanics - B/Fluids* 46 (2014). Updated version of previously published research report, pp. 82–96. DOI: `10.1016/j.euromechflu.2014.02.009`. URL: `https://hal.inria.fr/inria-00520612`.

[8] A. Collin and S. Imperiale. 'Mathematical analysis and 2-scale convergence of a heterogeneous microscopic bidomain model'. In: *Mathematical Models and Methods in Applied Sciences* (2018). URL: `https://hal.inria.fr/hal-01759914`.

[9] B. Lynch, S. Bancelin, C. Bonod-Bidaud, J.-B. Gueusquin, F. Ruggiero, M.-C. Schanne-Klein and J.-M. Allain. 'A novel microstructural interpretation for the biomechanics of mouse skin derived from multiscale characterization'. In: *Acta Biomaterialia* 50 (2017), pp. 302–311. DOI: `10.1016/j.actbio.2016.12.051`. URL: `https://hal.archives-ouvertes.fr/hal-01531321`.

[10] P. Moireau. 'Discrete-time formulations as time discretization strategies in data assimilation'. In: *Handbook of Numerical Analysis, Numerical Control: Part B*. Handbook of Numerical Analysis. Elsevier, 2022. DOI: `10.1016/bs.hna.2022.11.005`. URL: `https://hal.inria.fr/hal-03921465`.

[11] M. Sermesant, R. Chabiniok, P. Chinchapatnam, T. Mansi, F. Billet, P. Moireau, J.-M. Peyrat, K. C. Wong, J. Relan, K. S. Rhode, M. Ginks, P. Lambiase, H. Delingette, M. Sorine, C. A. Rinaldi, D. Chapelle, R. Razavi and N. Ayache. 'Patient-Specific Electromechanical Models of the Heart for Prediction of the Acute Effects of Pacing in CRT: a First Validation'. English. In: *Medical Image Analysis* 16.1 (2012), pp. 201–215. DOI: `10.1016/j.media.2011.07.003`. URL: `http://hal.inria.fr/inria-00616191`.

12.2 Publications of the year

International journals

[12] M. Aussal and P. Moireau. 'Kernel representation of Kalman observer and associated H-matrix based discretization'. In: *ESAIM: Control, Optimisation and Calculus of Variations* 28 (2022), p. 78. DOI: `10.1051/cocv/2022071`. URL: `https://hal.science/hal-03911500`.

[13] M. Barré, C. Grandmont and P. Moireau. 'Analysis of a linearized poromechanics model for incompressible and nearly incompressible materials'. In: *Evolution Equations and Control Theory* (2022). URL: `https://hal.inria.fr/hal-03501526`.

[14] A. Beni-Hamad, G. Beck, S. Imperiale and P. Joly. 'An efficient numerical method for time domain electromagnetic wave propagation in co-axial cables'. In: *Computational Methods in Applied Mathematics* (9th June 2022). URL: `https://hal.archives-ouvertes.fr/hal-03408400`.

[15] E. Berberoğlu, C. Stoeck, S. Kozerke and M. Genet. 'Quantification of left ventricular strain and torsion by joint analysis of 3D tagging and cine MR images'. In: *Medical Image Analysis* (2022). DOI: `10.1016/j.media.2022.102598`. URL: `https://hal.archives-ouvertes.fr/hal-03604931`.

[16] R. Chabiniok, B. Burtschell, D. Chapelle and P. Moireau. 'Dimensional reduction of a poromechanical cardiac model for myocardial perfusion studies'. In: *Applications in Engineering Science* 12 (14th Nov. 2022), p. 100121. DOI: `10.1016/j.apples.2022.100121`. URL: `https://hal.inria.fr/hal-03877604`.

[17] A. Collin, B. P. Hejblum, C. Vignals, L. Lehot, R. Thiébaut, P. Moireau and M. Prague. 'Using Population Based Kalman Estimator to Model COVID-19 Epidemic in France: Estimating the Effects of Non-Pharmaceutical Interventions on the Dynamics of Epidemic'. In: *International Journal of Biostatistics* (2022). URL: `https://hal.inria.fr/hal-03478094`.

[18] A. Collin, M. Prague and P. Moireau. 'Estimation for dynamical systems using a population-based Kalman filter – Applications in computational biology'. In: *MathematicS In Action* (11th Apr. 2022). DOI: 10.5802/msia.25. URL: https://hal.inria.fr/hal-02869347.

[19] C. Dupont, M. Vidrascu, P. Le Tallec, D. Barthès-Biesel and A.-V. Salsac. 'Modelling the fluid-structure interactions of a capsule using a nonlinear thin shell model: effect of wall thickness'. In: *Journal of Fluids and Structures* 113.103658 (2022). URL: https://hal.utc.fr/hal-03409766.

[20] C. Giraudet, J. Diaz, P. Le Tallec and J.-M. Allain. 'Multiscale mechanical model based on patient-specific geometry: application to early keratoconus development'. In: *Journal of the mechanical behavior of biomedical materials* 129 (May 2022), p. 105121. DOI: 10.1016/j.jmbbm.2022.105121. URL: https://hal.archives-ouvertes.fr/hal-03437194.

[21] M. Gusseva, D. Castellanos, J. Greer, M. Hussein, K. Hasbani, G. Greil, S. Reddy, M. Hussain, D. Chapelle and R. Chabiniok. 'Time-synchronization of interventional cardiovascular magnetic resonance data using a biomechanical model for pressure-volume loop analysis'. In: *Journal of Magnetic Resonance Imaging* 57.1 (1st Jan. 2023), pp. 320–323. DOI: 10.1002/jmri.28216. URL: https://hal.archives-ouvertes.fr/hal-03651166.

[22] F. Kimmig, M. Caruel and D. Chapelle. 'Varying thin filament activation in the framework of the Huxley'57 model'. In: *International Journal for Numerical Methods in Biomedical Engineering* (2022). DOI: 10.1002/cnm.3655. URL: https://hal.archives-ouvertes.fr/hal-03788978.

[23] B. Leturcq, P. Le Tallec, S. Pascal, O. Fandeur and N. Lamorte. 'A new reduced order model to represent the creep induced fuel assembly bow in PWR cores'. In: *Nuclear Engineering and Design* 394 (Aug. 2022), p. 111828. DOI: 10.1016/j.nucengdes.2022.111828. URL: https://hal.archives-ouvertes.fr/hal-03692909.

[24] C. Patte, P.-Y. Brillet, C. Fetita, J. F. Bernaudin, T. Gille, H. Nunes, D. Chapelle and M. Genet. 'Estimation of regional pulmonary compliance in idiopathic pulmonary fibrosis based on personalized lung poromechanical modeling'. In: *Journal of Biomechanical Engineering* 144.9 (Sept. 2022), 091008:1–091008:14. DOI: 10.1115/1.4054106. URL: https://hal.archives-ouvertes.fr/hal-03605865.

[25] C. Patte, M. Genet and D. Chapelle. 'A quasi-static poromechanical model of the lungs'. In: *Biomechanics and Modeling in Mechanobiology* 21.2 (Apr. 2022), pp. 527–551. DOI: 10.1007/s10237-021-01547-0. URL: https://hal.inria.fr/hal-03474200.

[26] N. Tueni, J.-M. Allain and M. Genet. 'On the structural origin of the anisotropy in the myocardium: Multiscale modeling and analysis'. In: *Journal of the mechanical behavior of biomedical materials* (Dec. 2022). URL: https://hal.archives-ouvertes.fr/hal-03604234.

[27] I. Vignon-Clémentel, D. Chapelle, P. Moireau, A. I. Barakat, A. Bel-Brunon and E. Vibert. 'Special Issue of the VPH2020 Conference: "Virtual Physiological Human: When Models, Methods and Experiments Meet the Clinic"'. In: *Annals of Biomedical Engineering* 50.5 (2022), pp. 483–484. DOI: 10.1007/s10439-022-02943-y. URL: https://hal.archives-ouvertes.fr/hal-03659783.

Scientific book chapters

[28] P. Moireau. 'Discrete-time formulations as time discretization strategies in data assimilation'. In: *Handbook of Numerical Analysis, Numerical Control: Part B.* Handbook of Numerical Analysis. Elsevier, 2022. DOI: 10.1016/bs.hna.2022.11.005. URL: https://hal.inria.fr/hal-03921465.

Doctoral dissertations and habilitation theses

[29] M. Genet. 'Some contributions to cardiac and pulmonary biomechanical modeling, simulation & estimation'. Institut Polytechnique de Paris, 21st June 2022. URL: https://hal.archives-ouvertes.fr/tel-03698102.

[30] M. Gusseva. ‘Patient-specific cardiovascular biomechanical modeling to augment interpretation of clinical data and assist planning interventions for patients with congenital heart disease’. Institut Polytechnique de Paris, 24th Mar. 2022. URL: https://theses.hal.science/tel-03683556.

[31] S. Imperiale. ‘Méthodes mathématiques et numériques pour des problèmes depropagation d’ondes double échelles’. Institut polytechnique de Paris, 27th Sept. 2022. URL: https://hal.inria.fr/tel-03944626.

Reports & preprints

[32] M. Barré and P. Ciarlet. *The T-coercivity approach for mixed problems*. 19th Oct. 2022. URL: https://hal.archives-ouvertes.fr/hal-03820910.

[33] L.-P. Chaintron, M. Caruel and F. Kimmig. *Modeling acto-myosin interaction: beyond the Huxley–Hill framework*. 20th June 2022. URL: https://hal.archives-ouvertes.fr/hal-03699263.

[34] L.-P. Chaintron, Á. Mateos González, L. Mertz and P. Moireau. *Mortensen Observer for a class of variational inequalities - Lost equivalence with stochastic filtering approaches*. 4th May 2022. URL: https://hal.inria.fr/hal-03659066.

[35] J. Dubois, S. Imperiale, A. Mangeney, F. Bouchut and J. Sainte-Marie. *Acoustic and gravity waves in the ocean: a new derivation of a linear model from the compressible Euler equation*. 1st Dec. 2022. URL: https://hal.archives-ouvertes.fr/hal-03880423.

[36] M. Genet, J. Diaz, D. Chapelle and P. Moireau. *Reduced left ventricular dynamics modeling based on a cylindrical assumption*. 27th Oct. 2022. URL: https://hal.archives-ouvertes.fr/hal-03832575.

[37] H. Gharbi, W. Wenlong, C. Giraudet, J.-M. Allain and E. Vennat. *Measure of the hygroscopic expansion of human dentin*. 22nd Nov. 2022. URL: https://hal.archives-ouvertes.fr/hal-03865668.

[38] D. Sabbagh, J. Cartailler, C. Touchard, J. Joachim, A. Mebazaa, F. Vallée, É. Gayat, A. Gramfort and D. Engemann. *Repurposing EEG monitoring of general anaesthesia for building biomarkers of brain ageing: An exploratory study*. 18th May 2022. DOI: 10.1101/2022.05.05.22274610. URL: https://hal.inria.fr/hal-03671308.